IN THE CLAIMS

Listing of the Claims

Cancel claims 1-34.

35. (new) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within the cell;

b) a 3' splice region comprising a branch point and a 3' splice acceptor site;

c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

36. (new) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within the cell;

(b) a 3' splice acceptor site;

(c) a spacer region that separates the 3' splice region from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

37. (new) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within the cell;

(b) a 5' splice site;

(c) a spacer region that separates the 5' splice site from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

38. (new) The cell of claim 35 wherein the nucleic acid molecule further comprises a 5' donor site.

39. (new) The cell of claim 35 wherein the 3' splice region further comprises a pyrimidine tract.

40. (new) The cell of claim 35, 36 or 37 wherein said nucleic acid molecule further comprises a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 5' splice site.

41. (new) The cell of Claim 35, 36 or 37 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

42. (new) The cell of Claim 35 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

43. (new) The cell of Claim 35 wherein the nucleotide sequences to be *trans*-spliced to the target pre mRNA encodes a factor VIII polypeptide.

44. (new) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within the cell;

(b) a 3' splice region comprising a branch point and a 3' splice acceptor site;

(c) a spacer region that separates the 3' splice region from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

45. (new) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within the cell;

(b) a 3' splice acceptor site;

(c) a spacer region that separates the 3' splice region from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

46. (new) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within the cell;

(b) a 5' splice site;

(c) a spacer region that separates the 5' splice site from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

47. (new) The cell of claim 44 wherein the nucleic acid molecule further comprises a 5' donor site.

48. (new ) The cell of claim 44 wherein the 3' splice region further comprises a pyrimidine tract.

49. (new) The cell of Claim 44, 45, or 46 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

50. (new) A method of producing a chimeric RNA molecule in a cell comprising: contacting a target factor non-humanVIII pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within the cell;

(b) a 3' splice region comprising a branch point and a 3' splice acceptor site;

(c) a spacer region that separates the 3' splice region from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

under conditions in which a portion of the nucleic acid molecule is *trans*-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

51. (new) A method of producing a chimeric RNA molecule in a cell comprising: contacting a non-human target factor VIII pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within the cell;

(b) a 3' splice acceptor site;

(c) a spacer region that separates the 3' splice region from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

under conditions in which a portion of the nucleic acid molecule is *trans*-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

52. (new) A method of producing a chimeric RNA molecule in a cell comprising: contacting a non-human target factor VIII pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within the cell;

(b) a 5' splice site;

(c) a spacer region that separates the 5' splice site from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

53. (new)The method of claim 50 wherein the nucleic acid molecule further comprises a 5' donor site.

54. (new)The method of claim 50 wherein the 3' splice region further comprises a pyrimidine tract.

55. (new) The method of claim 50, 51 or 52 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

56. (new) The method of Claim 50 wherein the nucleotide sequences to be *trans*-spliced to the target pre-mRNA encodes a factor VIII polypeptide.

57. (new) A nucleic acid molecule comprising:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within a cell;

(b) a 3' splice region comprising a branch point and a 3' splice acceptor site;

(c) a spacer region that separates the 3' splice region from the target binding domain; and

(d) a nucleotide sequence to be trans-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

58. (new) A nucleic acid molecule comprising:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within a cell;

(b) a 3' splice acceptor site;

(c) a spacer region that separates the 3' splice region from the target binding domain; and

(d) a nucleotide sequence to be trans-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

59. (new) A nucleic acid molecule comprising :

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within a cell;

(b) a 5' splice site;

(c) a spacer region that separates the 5' splice site from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

60. (new) The nucleic acid molecule of claim 57 wherein the nucleic acid molecule further comprises a 5' donor site.

61. (new) The nucleic acid molecule of claim 57 wherein the 3' splice region further comprises a pyrimidine tract.

62. (new) The nucleic acid molecule of claim 57, 58, or 59 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

63. (new) The nucleic acid molecule of claim 57, 58, 59 or 60 wherein the binding of the nucleic acid molecule to the target non-human factor VIII pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

64. (new) The nucleic acid molecule of claim 57, 58, 59 or 60 wherein the nucleotide sequences to be trans-spliced to the target pre mRNA encodes a factor VIII polypeptide.

65. (new) A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within a cell;

(b) a 3' splice region comprising a branch point and a 3' splice acceptor site;

(c) a spacer region that separates the 3' splice region from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

66. (new) A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within a cell;

(b) a 3' splice acceptor site;

(c) a spacer region that separates the 3' splice region from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

67. (new) A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within a cell;

(b) a 5' splice site;

(c) a spacer region that separates the 5' splice site from the target binding domain; and

(d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

68. (new) The vector of claim 65 wherein the nucleic acid molecule further comprises a 5' donor site.

69. (new) The vector of claim 65 wherein the nucleic acid molecule further comprises a pyrimidine tract.

70. (new) The vector of claim 65, 66, 67, or 68 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

71. (new) The vector of claim 65, 66, 67, or 68 wherein said vector is a viral vector.

72. (new) The vector of claim 65, 66, 67, or 68 wherein expression of the nucleic acid molecule is controlled by a liver cell specific promoter.

73. (new) A composition comprising a physiologically acceptable carrier and a nucleic acid molecule according to any of claims 57-64.

74. (new) A method for correcting a factor VIII genetic defect in a non-human subject comprising administering to said subject a nucleic acid molecule comprising:

(a) one or more target binding domains that target binding of the nucleic acid molecule to a non-human factor VIII pre-mRNA expressed within a cell wherein said pre-mRNA is encoded by a gene containing a factor VIII genetic defect; and

(b) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a factor VIII polypeptide;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

75. (new) The cell of claim 49 wherein said nucleic acid further comprises a safety sequence.

76. (new) The method of claim 54 and 55 wherein said nucleic acid further comprises a safety sequence.

77. (new) The nucleic acid molecule of claim 62 wherein said nucleic acid further comprises a safety sequence.

78. (new) The vector of claim 70 wherein said nucleic acid further comprises a safety sequence.

79. (new) The viral vector of claim 37, wherein the viral vector is an adeno-associated virus.